Citation:

Cross AJ, Leitzmann MF, Gail MH, Hollenbeck AR, Schatzkin A, Sinha R. A prospective study of red and processed meat intake in relation to cancer risk. PLoS Med. 2007;4(12):e325.

PubMed ID: 18076279

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

This prospective study investigated whether red or processed meat intake increases cancer risk at a variety of sites.

Inclusion Criteria:

- Men and women aged 50-71 yr who were members of AARP
- from six states: California, Florida, Louisana, New Jersey, North Carolina, and Pennsylvania and two metropolitan areas: Atlanta, Georgia and Detroit, Michigan

Exclusion Criteria:

- Individuals with duplicate records
- Those who died before returning the baseline questionnaire
- Those who had zero person years of follow-up
- Those who moved out of the eight study areas before returning the questionnaire
- Those who requested to be withdrawn from the study,
- Those whose questionnaire was filled in by someone else on their behalf
- Those who had prevalent cancer at baseline.
- Those who had end-stage renal disease at baseline
- Those with extreme daily total energy intake or below the 25th percentile on the logarithmic scale

Description of Study Protocol:

Recruitment

Recruitment began in 1995 when a self-administered questionnaire eliciting information on demographic and lifestyle characteristics, including dietary habits, was mailed to 3.5 million

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members of AARP.

Design

Dietary intake was compared to data for cancer ascertainment.

Statistical Analysis

Cox proportional hazards regression was used to estimate hazard ratios and 95% confidence intervals within quintiles of red and processed meat intake.

Data Collection Summary:

Timing of Measurements

Baseline (1995-1996) to end of 2003

Dependent Variables

- Cancer case ascertainment: identified by linkage to state cancer registries and the National Death Index Plus. Cancer diagnoses contributed to the incidence of the tumor site of the first diagnosis only and not subsequent diagnoses for additional sites. Cancer sites include:
  - Oral cavity and pharyngeal
  - Laryngeal
  - Esophageal
  - Gastric
  - Colorectal
  - Liver
  - Pancreatic
  - Lung
  - Bladder
  - Kidney
  - Thyroid
  - Non-Hodgkin
  - lymphoma
  - Leukemia
  - Melanoma
  - Brain
  - Myeloma
  - Prostate
  - Breast
  - Endometrial
  - Ovarian
  - Cervical

Independent Variables

- Dietary Assessment: 124 item food frequency questionnaire (FFQ), based on the Diet History Qeustionnaire developed at the National Cancer Institute.
  - Red meat
  - Processed meat

Control Variables

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- Assessed via questionnaire: age, race, gender, marital status, positive family history of cancer, height, weight, smoking history, education, and physical activity.

Description of Actual Data Sample:

Initial N: 567,169 returned the baseline questionnaire

Attrition (final N): Analytic cohort: 494,036 (294,724 men and 199,312 women)

Age: over age 50

Ethnicity: primarily white

Other relevant demographics: primarily former smokers and non-smokers; primarily married

Anthropometrics men mean BMI 26.1-28.4; women mean BMI 25.4-28.2

Location:

California, Florida, Louisiana, New Jersey, North Carolina and Pennsylvania; Atlanta, Georgia and Detroit, Michigan

Summary of Results:

Key Findings

- In general, those in the highest quintile of red meat intake tended to slightly younger, less educated, less physically active and less likely to consume fruits, vegetables and alcohol than those in the lowest quintile.
- Those in the highest quintile of red meat intake were more likely to have a higher total energy intake, a higher BMI, and more likely to be a current smoker.
- Women in the highest quintile of red meat intake were also more likely to be married than those in the lowest quintile.
- Individuals in the highest quintile of red meat intake compared with those in the lowest, had a statistically significant elevated risk of several malignancies including: esophageal, colorectal, liver, lung, and borderline stastistical significance for laryngeal cancer.
- The positive association for red meat intake and colorectal cancer was due more to cancer of the rectum than the colon, marginally significant.
- Control for smoking did not alter the associations for cancers of the esophagus, colorectum, liver, lung or larynx.
- Red meat intake was not associated with gastric or bladder cancer, leukemia, lymphoma, or melanoma. Null findings also for sex-specific cancers: breast, ovarian, cervical and prostrate.
- Red meat intake was inversely associated with endometrial cancer.
- Red meat intake was positively associated with pancreatic cancer in men only.
- Leukemia and melanoma were inversely associated with processed meat intake.
- During a mean follow-up of 6.8 yrs, 5107 cases of colorectal cancer were observed.
- Individuals in the highest quintile of red met intake. Compared with those in lowest, had statistically significant elevated risk of colorectal cancer (multivariate HR = 1.24; 95% CI: 1.12, 1.36: P for trend < 0.001).
- Individuals in the highest quintile, compared with those in the lowest quintile, of processed meat intake were at elevated risk of colorectal (multivariate HR = 1.20; 95% CI: 1.09, 1.32; P for trend <0.001).

Author Conclusion:

A diet high in red or processed meat was associated with an elevated risk of both colorectal and lung cancer; in addition, red meat was associated with an elevated risk of esophageal and liver cancer.

Reviewer Comments:

The results did not adjust for multiple comparisons.

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Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A

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3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	Yes
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A

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6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes

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8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes

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